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## REMARKS

Claims 1-9 and 21-36 are pending in this application. The pending claims have been rejected based on several grounds as listed below.

1. Claims 1-5, 7-9, 21-26, and 33-34 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by the Bethell reference ("Bethell").
2. Claims 2, 4, 6, and 22 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Bethell, and in view of U.S. Patent No. 5,609,907 ("the Natan '907 patent").
3. Claims 27-32 and 35-36 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Bethell, and in view of the Terrill reference ("Terrill").

Applicants traverse each of these rejections and request their withdrawal.

### I. The Invention

Preliminarily, the invention enables investigation of a target environment to determine whether or in what amount a chemical species may be present. This is accomplished by exposing an article of manufacture comprising a multiplicity of particles in close-packed orientation to a target environment. Each particle has a core of conductive metal or metal alloy. Deposited on the core is a ligand shell capable of interacting with the chemical species of interest, such that a property of the multiplicity of particles, typically conductivity, is altered. Thus, the ligand shell is neither so thin that the multiplicity of particles is effectively metallic in conductivity properties, nor so thick as to be completely electrically insulating. The specification discloses a nanometer range ligand shell thickness. Claim 1 already recites that range, namely 0.4 to 4 nm; the other independent claims have been amended to prescribe same also (the insertion of the metal core diameter range in claims 21, 25, 33 and 34 is not for

patentability purposes, but solely to achieve uniformity). When the multiplicity of particles is subjected to conditions sufficient to alter the relevant property, which is monitored to determine any change, any attenuation of the property is an indication of whether, or in what amount, the species of interest is present.

The claims at issue are directed to either:

- i) an article of manufacture suitable for use in determining whether or in what amount a chemical species is present in a target environment (claims 1-9); or
- ii) an assembly suitable for (claims 21-26), a method of fabricating an assembly suitable for (claims 27- 32), a system suitable for (claim 33), or a system for (claims 34-36), investigating a target environment to determine whether or in what amount a chemical species may be present.

A key element in each of these claims is particles which have appropriate ligand shell dimensions.

## II. Novelty Over Bethell

For a reference to anticipate, it must contain all of the elements of the claim. *Hybritech Inc. v. Monoclonal Antibodies, Inc.* 802 F.2d 1367, 1379 (Fed. Cir. 1986); *In re Marshall*, 578 F.2d 301, 304 (C.C.P.A. 1978).

The specification of the invention teaches that, when the thickness of the ligand shell component of the particles recited in the claims is 0.4 to 4 nm, the shell is neither too thin (i.e., so thin that the multiplicity of particles is effectively metallic) nor too thick (i.e., so thick that there is complete electrical insulation). See page 13, lines 12-17. Claim 1 as originally filed contains that ligand shell prescription, and claims 21, 25, 33, and 34 have now been amended to conform. However, Bethell does not teach or disclose particles in which the ligand shell layer

has the required thickness, and thus cannot anticipate claims 1-5, 7-9, 21-26, and 33-34, which recite that prescription. Bethell is simply devoid of the necessary teaching.

Assuming *arguendo* that Bethell contains disclosure of an assembly of colloidal metal upon a surface linked by thiol groups, the reference is still deficient. Even if that concept is known, Bethell does not make attainment of the required ligand shell thickness inevitable. Moreover, even if the Bethell construct's conductivity may be measurable, there is no teaching that the metal core/ligand layer construct should be fabricated in a manner – i.e., with a ligand shell thickness of 0.4 to 4 nm – such that it functions as desired in the sensor applications for which the claimed embodiments are explicitly contemplated. Accordingly, the structures disclosed in Bethell do not inherently exhibit the features required for Applicants' invention, and thus if anyone practicing the Bethell disclosure had produced suitable particles it would have been an unrecognized accident. An accident or unwitting duplication of an invention cannot constitute anticipation. *In re Felton*, 179 U.S.P.Q. 295, 298 (C.C.P.A. 1973).

The rejection of Applicants' claims 1-5, 7-9, 21-26, and 33-34 under 35 U.S.C. § 102(b) is unjustified and should be withdrawn.

### III. Nonobviousness Over Bethell and the Natan '907 Patent

To establish *prima facie* obviousness of a claimed invention, the Examiner must show that one of ordinary skill would have been motivated by the prior art to fashion an embodiment satisfying all claim limitations. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974); MPEP § 2143.03.

Like Bethell, the Natan '907 patent fails to teach an assembly having particles in which the ligand shell thickness is proper. Rather, the assemblies disclosed in Natan involve the use of substances such as biotin and streptavidin to achieve the non-covalent attachment of metal core

particles. See Figures. Even (assuming *arguendo*) were the biotin or streptavidin to interact with the target species, it is not disclosed that the Natan construct is designed to nurture this interaction, and the alteration of a particle property as a consequence thereof, in accordance with Applicants' invention through provision of a ligand shell thickness between 0.4 and 4 nm. And, like Bethell, the Natan '907 patent's teaching also fails to make inevitable the attainment of a ligand shell with the specified thickness. In contrast, Applicants' invention provides particles with just such thickness values; it stands to reason that the interaction of target species with the ligand shell, and its effectiveness in altering a property of the particles, is reliably nurtured pursuant to Applicants' design. Bethell and the Natan '907 patent in combination fail to teach either expressly or inherently a construct in which the ligand layer is of the desired thickness.

Therefore, the Bethell reference and the Natan patents fail to provide the necessary incentive or motivation to produce the Applicants' invention as claimed. "The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggests the desirability of the modification." *In re Fritch*, 23 U.S.P.Q.2d 1780, 1783-1784 (Fed. Cir. 1992). It goes without saying that reference teachings which do not teach the invention inherently are not capable of supporting an obviousness rejection, since the required motivational disclosure is missing. *In re Felton, supra*.

Moreover, artificially excising only some aspects of the Natan '907 patent's teachings to formulate the rejection is impermissible. All the essential aspects of the reference teachings must be preserved in the combination. It is noted that Bethell teaches utilization of bonding groups, such as thiols, to adhere metal core bodies to a substrate. However, the Natan '907 patent teaches utilization of a substrate-mounted polymer layer as the immobilizing agent. The patent's teaching for a polymeric adherent layer is destroyed in the Examiner's rejection, because

that teaching is ignored in an attempt to put forth an internally consistent position on how the invention - which does not have a polymeric adherent layer - is foreshadowed by the art. A combination of teachings that destroys a basic aspect of the Natan subject matter is improper. See *Ex parte Hartmann*, 186 U.S.P.Q. 366, 367 (Bd. Pat. App. & Int. 1974).

The rejection under 35 U.S.C. § 103(a) should be withdrawn.

#### IV. Nonobviousness Over Bethell and Terrill

As explained *supra* (Section II), Bethell does not disclose a structure that meets the limitations of the Applicants' claims. In addition, as explained *supra* (Section III), Bethell, in combination with the Natan patents, fails to teach or suggest a structure that meets the limitations of the Applicants' claims.

The particles, and other embodiments incorporating them, defined in Applicants' claims would not have been obvious to one of ordinary skill in the art. The apparatus and other teachings of Terrill would not have been sufficient in combination with the other references to yield a result that meets the unique limitations of Applicants' claims; Terrill does not teach the prescribed ligand shell thickness.

#### V. Natan '202 Patent

U.S. Patent No. 6,025,202 ("the Natan '202 patent") was cited in Applicants' Information Disclosure Statement. This patent is inadequate to add, to the references on which the rejections are already based, anything that would have made the instant invention obvious.

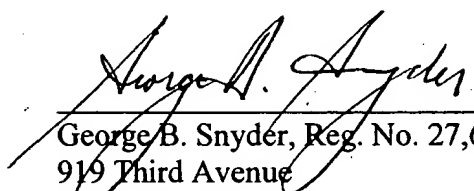
VI. Conclusion

For the reasons set forth above, Applicants respectfully submit that claims 1-9 and 21-36 are patentable over the art of record and in condition for allowance. If there are any remaining issues that would prevent the allowance of these claims, the Examiner is respectfully asked to contact the Applicants' undersigned attorney.

No fee is believed due. The Assistant Commissioner is authorized to charge any deficiency or credit any overpayment to our Deposit Account No. 50-0540.

Respectfully submitted,

KRAMER LEVIN NAFTALIS & FRANKEL LLP  
Attorneys for Applicants



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George B. Snyder, Reg. No. 27,675  
919 Third Avenue  
New York, NY 10022  
Phone: (212) 715-9100  
Fax: (212) 715-8000



APPENDIX A

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21. (Amended) An assembly suitable for investigation of a target environment to determine whether or in what amount a chemical species may be present, which comprises

(a) a substrate suitably configured for presenting a multiplicity of particles supported thereon to contact with said environment;

(b) supported by said substrate, a multiplicity of particles in close-packed orientation, said particles having a core of conductive metal or conductive metal alloy, in each said particle such core being of 0.8 to 40.0 nm in maximum dimension, and deposited thereon a ligand, of thickness from 0.4 to 4.0 nm, which is capable of interacting with said species such that a property of said multiplicity of particles is altered; and

(c) a sensor for monitoring said property of said multiplicity of particles.

25. (Amended) An assembly suitable for investigating a target environment, to determine whether or in what amount a chemical species may be present, which comprises

(a) a substrate suitably configured for presenting a multiplicity of particles supported thereon to contact with said species;

(b) supported by said substrate, said multiplicity of particles having a core of conductive metal or conductive metal alloy, in each said particle such core being of 0.8 to 40.0 nm in maximum dimension, and deposited thereon a ligand, of thickness from 0.4 to 4.0 nm, which is capable of interacting with said species such that the electrical conductivity of particles is altered;

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(c) a pair of electrodes, each in electrical contact with said multiplicity of particles; and

(d) a sensor for monitoring the electrical conductivity of said multiplicity of particles to determine whether there is, or the amount of, any change in said conductivity as an indication of whether or in what amount said species is present.

33. (Amended) A system suitable for investigating a target environment to determine whether or in what amount a chemical species may be present, which comprises

(a) a multiplicity of particles in close-packed orientation, said particles having a core of conductive metal or conductive metal alloy, in each said particle such core being of 0.8 to 40.0 nm in maximum dimension, and deposited thereon a ligand, of thickness from 0.4 to 4.0 nm, which is capable of interacting with said species such that a property of said multiplicity of particles is altered;

(b) means for exposing said multiplicity of particles to said environment;

(c) means for subjecting said multiplicity of particles to conditions sufficient for said property to be exhibited; and

(d) means for monitoring said property to determine whether there is, or the amount of, any change in such property as an indication of whether or in what amount said species is present.

34. (Amended) A system for investigating a target environment to determine whether or in what amount a chemical species may be present, which comprises

(a) a multiplicity of particles in close-packed orientation, said particles having a core of conductive metal or conductive metal alloy, in each said particle such core being of 0.8 to 40.0 nm in maximum dimension, and deposited thereon a ligand, of thickness from 0.4 to 4.0

nm, which is capable of interacting with said species such that the electrical resistivity of said multiplicity of particles is altered;

(b) means for exposing said multiplicity of particles to said environment;

(c) means for passing an electrical current through said multiplicity of particles; and

(d) means for monitoring the electrical resistivity of said multiplicity of particles to determine whether there is, or the amount of, any change in said resistivity as an indication of whether or in what amount said species is present.